**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
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| 9823102.0 | 23 October 1998 (23.10.98) | GB |
| 9823101.2 | 23 October 1998 (23.10.98) | GB |

(71) Applicant *(for GB only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for all designated States except GB US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

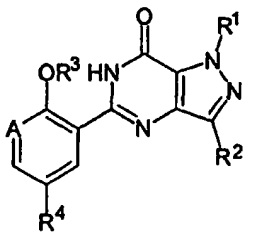
(75) Inventors/Applicants *(for US only)*: BUNNAGE, Mark, Edward [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). MAW, Graham, Nigel [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). RAWSON, David, James [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). WOOD, Anthony [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). MATHIAS, John, Paul [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). STREET, Stephen, Derek, Albert [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: SPIEGEL, Allen, J. et al.; c/o Simpson, Alison, Urquhart-Dykes & Lord, 91 Wimpole Street, London W1M 8AH (GB).

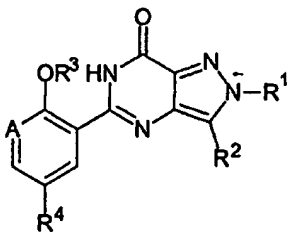
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*

(54) Title: PYRAZOLOPYRIMIDINONE cGMP PDE5 INHIBITORS FOR THE TREATMENT OF SEXUAL DYSFUNCTION




(IA)




(IB)

(57) Abstract

There is provided compounds of formula (IA) and of formula (IB), wherein $R^1$, $R^2$, $R^3$, $R^4$ and A have meanings given in the description, which are useful in the curative and prophylactic treatment of medical conditions for which inhibition of a cyclic guanosine 3',5'–monophosphate phosphodiesterase (e.g. cGMP PDE5) is desired.

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(21) International Application Number: PCT/IB02/04426

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(30) Priority Data:
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(71) Applicant *(for GB only)*: **PFIZER LIMITED** [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

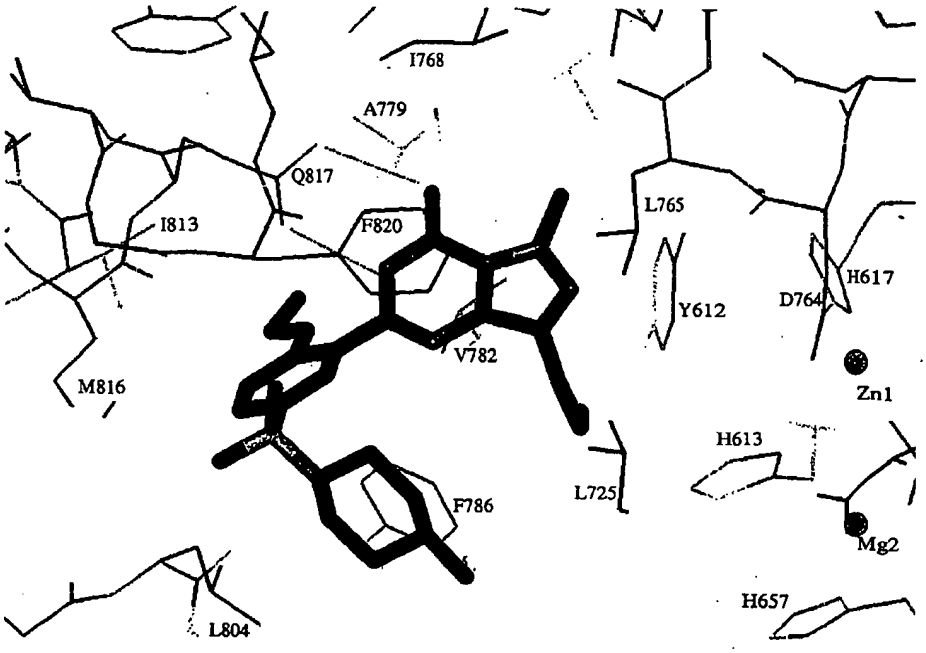
(71) Applicant *(for all designated States except GB, US)*: **PFIZER INC.** [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BROWN, David, Graham** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **GROOM, Colin, Roger** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **HOPKINS, Andrew, Lee** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **JENKINS, Timothy, Mark** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **KAMP, Sarah, Helen** [GB/GB]; U.K. Patent Department, Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **O'GARA, Margaret, Mary** [IE/FR]; Pfizer Global Research and Development, 3-9, rue de la Loge, B.P. 100, F-94265 Fresnes Cedex (FR). **RINGROSE, Heather, Joan** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **ROBINSON, Colin, Mark** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **TAYLOR, Wendy, Elaine** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

*[Continued on next page]*

(54) Title: CRYSTAL STRUCTURE OF PHOSPHODIESTERASE 5 AND USE THEREOF




(57) Abstract: The present invention relates , *inter alia* to the crystal structures of a phosphodiesterase 5 (PDE5) and PDE5/PDE5 ligand complex and their uses in identifying PDE5 ligands, including PDE5 inhibitor compounds. The present invention also relates to methods of identifying such PDE5 inhibitor compounds and their medical use. Also contemplated by the present invention are crystals of PDE5/PDE5 inhibitor complexes.



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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

| (51) International Patent Classification 5 : | A1 | (11) International Publication Number: WO 93/06104 |
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(21) International Application Number: PCT/EP92/02068

(22) International Filing Date: 4 September 1992 (04.09.92)

(30) Priority data:
9119704.6 14 September 1991 (14.09.91) GB

(71) Applicant *(for GB IE only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for all designated States except GB IE US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

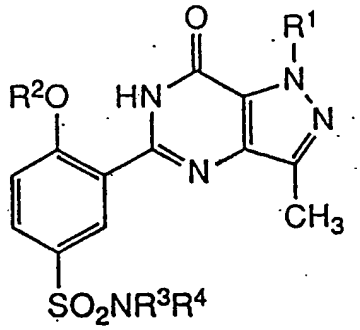
(72) Inventors; and
(75) Inventors/Applicants *(for US only)* : BROWN, David [GB/GB]; TERRETT, Nicholas, Kenneth [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: MOORE, James, William et al.; Pfizer Limited, Patents Department, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(81) Designated States: CA, FI, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE).

Published
*With international search report.*

(54) Title: PYRAZOLOPYRIMIDINONE ANTIANGINAL AGENTS




(I)

(57) Abstract

Compounds of formula (I) and pharmaceutically acceptable salts thereof, wherein $R^1$ is methyl or ethyl; $R^2$ is ethyl or n-propyl; and $R^3$ and $R^4$ are each independently H, or $C_1$-$C_6$ alkyl optionally substituted with $C_5$-$C_7$ cycloalkyl or with morpholino; are selective cGMP PDE inhibitors useful in the treatment of cardiovascular disorders such as angina, hypertension, heart failure and atherosclerosis.

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国 際 事 務 局

PCT

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| (51) 国際特許分類 5<br>C07D 215/00, 215/00, 235/00<br>C07D 239/72, 239/84, 239/94<br>C07D 239/95, A61K 31/47<br>A61K 31/505 | A1 | (11) 国際公開番号 | WO 93/07124 |
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特願平3/320853 1991年9月30日(30. 09. 91) JP

(71) 出願人(米国を除くすべての指定国について)
エーザイ株式会社(EISAI CO., LTD.)〔JP/JP〕
〒112-88 東京都文京区小石川4丁目6番10号 Tokyo, (JP)
(72) 発明者;および
(75) 発明者/出願人(米国についてのみ)
高瀬保孝(TAKASE, Yasutaka)〔JP/JP〕
〒305 茨城県つくば市春日4-19-13 エーザイ紫山寮308 Ibaraki, (JP)
渡辺信久(WATANABE, Nobuhisa)〔JP/JP〕
〒305 茨城県つくば市天久保2-23-5 メゾン学園105 Ibaraki, (JP)
松井 皓(MATSUI, Makoto)〔JP/JP〕
〒466 愛知県名古屋市昭和区山里町69番地 Aichi, (JP)
生田博寛(IKUTA, Hironori)〔JP/JP〕
〒300-12 茨城県牛久市栄町2-35-12 Ibaraki, (JP)
木村禎治(KIMURA, Teiji)〔JP/JP〕
〒305 茨城県つくば市梅園2-16-1 ルンビーニ梅園604 Ibaraki, (JP)
佐伯隆生(SAEKI, Takao)〔JP/JP〕
〒302-01 茨城県北相馬郡守谷町松前台2-9-6 Ibaraki, (JP)
足立秀之(ADACHI, Hideyuki)〔JP/JP〕
〒300-03 茨城県稲敷郡阿見町中央7-7-18 Ibaraki, (JP)
徳村忠一(TOKUMURA, Tadakazu)〔JP/JP〕
〒300 茨城県土浦市桜ヶ丘町32-5 Ibaraki, (JP)
餅田久利(MOCHIDA, Hisatoshi)〔JP/JP〕
〒483 愛知県江南市藤ヶ丘7-1-2 江南団地216-106 Aichi, (JP)
秋田靖典(AKITA, Yasunori)〔JP/JP〕
〒300-24 茨城県筑波郡谷和原村下小目122 Ibaraki, (JP)
左右田茂(SOUDA, Shigeru)〔JP/JP〕
〒300-12 茨城県牛久市牛久町1687-21 Ibaraki, (JP)
(74) 代理人
弁理士 古谷 馨, 外(FURUYA, Kaoru et al.)
〒103 東京都中央区日本橋堀留町1-8-11 日本橋TMビル Tokyo, (JP)

(81) 指定国
AT(欧州特許), AU, BE(欧州特許), CA, CH(欧州特許), DE(欧州特許), DK(欧州特許), ES(欧州特許), FI, FR(欧州特許), GB(欧州特許), GR(欧州特許), HU, IE(欧州特許), IT(欧州特許), JP, KR, LU(欧州特許), NL(欧州特許), NO, RU, SE(欧州特許), US.

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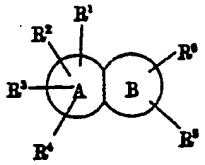
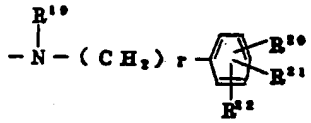
(54) Title : NITROGENOUS HETEROCYCLIC COMPOUND

(54) 発明の名称 含窒素複素環化合物




(I)




(a)

(57) Abstract

A nitrogenous heterocyclic compound represented by general formula (I) or a pharmacologically acceptable salt thereof, efficacious in treating various ischemic cardiac diseases, wherein ring A represents a benzene, pyridine or cyclohexane ring; ring B represents a pyridine, pyrimidine or imidazole ring; $R^1$, $R^2$, $R^3$ and $R^4$ represent each hydrogen, halogen, lower alkoxy, etc.; $R^5$ represents $-NR^{11}R^{12}$ (wherein $R^{11}$ and $R^{12}$ represent each hydrogen, lower alkyl, etc.), etc.; and $R^6$ represents (a) (wherein $R^{19}$ represents hydrogen, lower alkyl, etc.; $R^{20}$, $R^{21}$ and $R^{22}$ represent each hydrogen, halogen, hydroxy, etc.; and r represents an integer of 0.1 to 8), etc.

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(51) International Patent Classification 5 :
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A1

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(30) Priority data:
9121028.6 3 October 1991 (03.10.91) GB

(71) Applicant *(for GB IE only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for all designated States except GB IE US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, N.Y. 10017 (US).

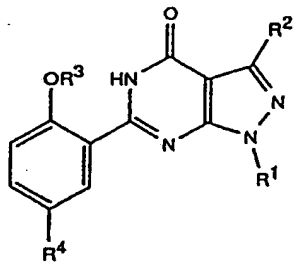
(72) Inventors; and
(75) Inventors/Applicants *(for US only)* : BELL, Andrew, Simon [GB/GB]; TERRETT, Nicholas, Kenneth [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: MOORE, James, William et al.; Pfizer Limited, Patents Department, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(81) Designated States: CA, FI, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE).

**Published**
*With international search report.*

(54) Title: PYRAZOLOPYRIMIDINONE ANTIANGINAL AGENTS




(I)

(57) Abstract

Compounds of formula (I), and pharmaceutically acceptable salts thereof wherein $R^1$ is $C_1$-$C_6$ alkyl; $R^2$ is H, methyl or ethyl; $R^3$ is $C_2$-$C_4$ alkyl; $R^4$ is $C_1$-$C_4$ alkyl optionally substituted with $NR^5R^6$, CN, $CONR^5R^6$ or $CO_2R^7$; $C_2$-$C_4$ alkenyl optionally substituted with CN, $CONR^5R^6$ or $CO_2R^7$; $C_2$-$C_4$ alkanoyl optionally substituted with $NR^5R^6$; $SO_2NR^5R^6$; $CONR^5R^6$; $CO_2R^7$; or halo; $R^5$ and $R^6$ are each independently H or $C_1$-$C_4$ alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidino, piperidino, morpholino, 4-($NR^8$)-1-piperazinyl or 1-imidazolyl group wherein said group is optionally substituted by one or two $C_1$-$C_4$ alkyl groups; $R^7$ is H or $C_1$-$C_4$ alkyl; and $R^8$ is H, $C_1$-$C_3$ alkyl or hydroxy $C_2$-$C_3$ alkyl; are selective cGMP PDE inhibitors useful in the treatment of cardiovascular disorders such as angina hypertension, heart failure and atherosclerosis.

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(71) Applicant *(for GB IE only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for all designated States except GB IE US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : TERRETT, Nicholas, Kenneth [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: MOORE, James, William et al.; Pfizer Limited, Patents Department, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(81) Designated States: CA, FI, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

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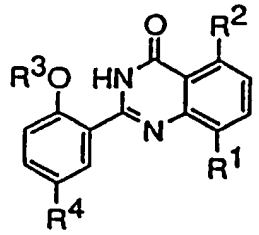
(54) Title: QUINAZOLINONE ANTIANGINAL AGENTS



(I)

(57) Abstract

Compounds of formula (I) and pharmaceutically acceptable salts thereof wherein $R^1$ is H, $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy or $CONR^5R^6$; $R^2$ is H or $C_1$-$C_4$ alkyl; $R^3$ is $C_2$-$C_4$ alkyl; $R^4$ is H, $C_2$-$C_4$ alkanoyl optionally substituted with $NR^7R^8$, (hydroxy)$C_2$-$C_4$ alkyl optionally substituted with $NR^7R^8$, $CH=CHCO_2R^9$, $CH=CHCONR^7R^8$, $CH_2CH_2CO_2R^9$, $CH_2CH_2CONR^7R^8$, $SO_2NR^7R^8$, $SO_2NH(CH_2)_nNR^7R^8$ or imidazolyl; $R^5$ and $R^6$ are each independently H or $C_1$-$C_4$ alkyl; $R^7$ and $R^8$ are each independently H or $C_1$-$C_4$ alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidino, piperidino, morpholino or 4-($NR^{10}$)-1-piperazinyl group wherein any of said groups is optionally substituted with $CONR^5R^6$; $R^9$ is H or $C_1$-$C_4$ alkyl; $R^{10}$ is H, $C_1$-$C_3$ alkyl or (hydroxy)$C_2$-$C_3$ alkyl; and n is 2, 3 or 4; with the proviso that $R^4$ is not H when $R^1$ is H, $C_1$-$C_4$ alkyl or $C_1$-$C_4$ alkoxy; are selective cGMP PDE inhibitors useful in the treatment of cardiovascular disorders such as angina, hypertension, heart failure and atherosclerosis.

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(30) Priority data:
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(71) Applicant *(for GB only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for JP only)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(71) Applicant *(for all designated States except GB JP US)*: PFIZER RESEARCH AND DEVELOPMENT COMPANY, N.V./S.A.[IE/IE]; Alexandra House, Earlsfort Centre, Earlsfort Terrace, Dublin (IE).

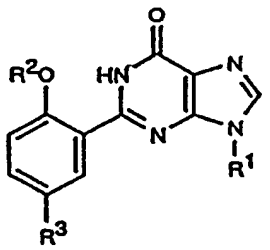
(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : TERRETT, Nicholas, Kenneth [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: MOORE, James, William et al.; Pfizer Limited, Patents Department, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(81) Designated States: CA, FI, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
*With international search report.*

(54) Title: PURINONE ANTIANGINAL AGENTS



(I)

(57) Abstract

Compounds of formula (I), and pharmaceutically acceptable salts thereof, wherein $R^1$ is $C_1$-$C_4$ alkyl; $R^2$ is $C_2$-$C_4$ alkyl; $R^3$ is H or $SO_2NR^4R^5$; $R^4$ and $R^5$ together with the nitrogen atom to which they are attached form a pyrrolidino, piperidino, morpholino or 4-N-($R^6$)-1-piperazinyl group; and $R^6$ is H or $C_1$-$C_3$ alkyl; are selective cGMP PDE inhibitors useful in the treatment of, *inter alia*, cardiovascular disorders such as angina, hypertension, heart failure and atherosclerosis.

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(71) Applicant *(for all designated States except US)*: LABORATOIRES GLAXO S.A. [FR/FR]; 42, rue Vineuse, F-75016 Paris (FR).

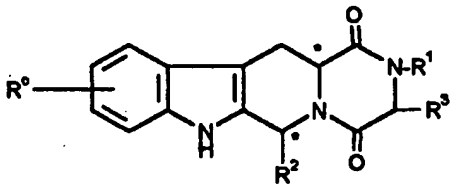
(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: DAUGAN, Alain, Claude-Marie [FR/FR]; Laboratoires Glaxo S.A., Centre de Recherches, Z.A. de Courtabœuf, 25, avenue de Québec, F-91940 Les Ulis (FR).

(74) Agents: GALLAFENT, Alison et al.; Glaxo plc, Glaxo House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ).

**Published**
*With international search report.*
*Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(54) Title: TETRACYCLIC DERIVATIVES, PROCESS OF PREPARATION AND USE




(I)


(a)

(57) Abstract

A compound of formula (I) and salts and solvates thereof, in which: $R^0$ represents hydrogen, halogen or $C_{1-6}$ alkyl; $R^1$ represents hydrogen, $C_{1-6}$alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halo$C_{1-6}$alkyl, $C_{3-8}$cycloalkyl, $C_{3-8}$cycloalkyl$C_{1-3}$alkyl, aryl$C_{1-3}$alkyl or heteroaryl$C_{1-3}$alkyl; $R^2$ represents an optionally substituted monocyclic aromatic ring selected from benzene, thiophene, furan and pyridine or an optionally substituted bicyclic ring (a) attached to the rest of the molecule via one of the benzene ring carbon atoms and wherein the fused ring (A) is a 5- or 6-membered ring which may be saturated or partially or fully unsaturated and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulphur and nitrogen; and $R^3$ represents hydrogen or $C_{1-3}$ alkyl, or $R^1$ and $R^3$ together represent a 3- or 4-membered alkyl or alkenyl chain. A compound of formula (I) is a potent and selective inhibitor of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase (cGMP specific PDE) having a utility in a variety of therapeutic areas where such inhibition is beneficial, including the treatment of cardiovascular disorders.

**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
**C12Q 1/68, C12P 19/34, G06T 1/00, 1/40, G06K 9/58, 9/40, 9/60, C07H 21/04, 19/04**

**A1**

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(43) International Publication Date: 13 June 1996 (13.06.96)

(21) International Application Number: PCT/US95/16155

(22) International Filing Date: 8 December 1995 (08.12.95)

(30) Priority Data:
08/353,018 9 December 1994 (09.12.94) US

(71) Applicants: THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 22nd floor, 300 Lakeside Drive, Oakland, CA 94612 (US). THE MEDICAL RESEARCH COUNCIL [GB/GB]; Hills Road, Cambridge CB2 2QH (GB).

(72) Inventors: PINKEL, Daniel; 31 Manzanita Court, Walnut Creek, CA 94595 (US). GRAY, Joe, W.; 50 Santa Paula Avenue, San Francisco, CA 94127 (US). ALBERTSON, Donna; 42 Glisson Road, Cambridge CB1 2HF (GB).

(74) Agents: BASTIAN, Kevin, L. et al.; Townsend and Townsend and Crew, Steuart Street Tower, One Market, San Francisco, CA 94105-1492 (US).

(81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
*With international search report.*

(54) Title: COMPARATIVE FLUORESCENCE HYBRIDIZATION TO NUCLEIC ACID ARRAYS

(57) Abstract

The present invention provides methods of determining relative copy number of target nucleic acids and precise mapping of chromosomal abnormalities associated with disease. The methods of the invention use target nucleic acids immobilized on a solid surface, to which a sample comprising two sets of differentially labeled nucleic acids are hybridized. The hybridization of the labeled nucleic acids to the solid surface is then detected using standard techniques.

**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
**C12N 15/54, 9/12, C12Q 1/68, C07K 16/40, C12N 5/12, G01N 33/68, C12Q 1/48, C07D 41/40, C07C 255/34, C07D 215/00, 239/72**

A2

(11) International Publication Number: **WO 96/18738**

(43) International Publication Date: 20 June 1996 (20.06.96)

(21) International Application Number: PCT/US95/15846

(22) International Filing Date: 6 December 1995 (06.12.95)

(30) Priority Data:

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|---|---|---|
| 08/357,642 | 15 December 1994 (15.12.94) | US |
| 08/460,626 | 2 June 1995 (02.06.95) | US |

(71) Applicants: SUGEN, INC. [US/US]; 515 Galveston Drive, Redwood City, CA 94063 (US). NEW YORK UNIVERSITY [US/US]; 550 First Avenue, New York, NY 10016 (US).

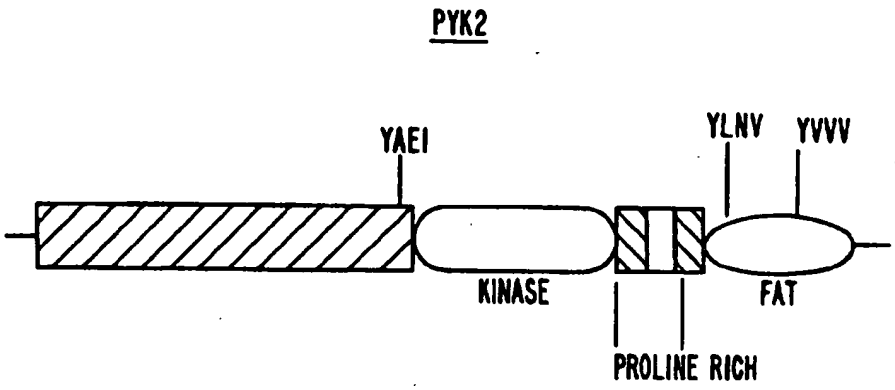
(72) Inventors: LEV, Sima; 8 Locksley Avenue #1C, San Francisco, CA 94122 (US). SCHLESSINGER, Joseph; 37 Washington Square, New York, NY 10011 (US).

(74) Agents: WARBURG, Richard, J. et al.; Lyon & Lyon, First Interstate World Center, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).

(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, LS, MW, SD, SZ, UG).

**Published**
*Without international search report and to be republished upon receipt of that report.*

(54) Title: PROBIN TYROSINE KINASE (PYK2) ITS cDNA CLONING AND ITS USES




(57) Abstract

The present invention features a method for treatment of an organism having a disease or condition characterized by an abnormality in a signal transduction pathway, wherein the signal transduction pathway includes a PYK2 protein. The invention also features methods for diagnosing such diseases and for screening for agents that will be useful in treating such diseases. The invention also features purified and/or isolated nucleic acid encoding a PYK2 protein.

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : B01J 19/00, C12Q 1/68 — A1

(11) International Publication Number: **WO 97/46313**

(43) International Publication Date: 11 December 1997 (11.12.97)

(21) International Application Number: PCT/US97/09902

(22) International Filing Date: 6 June 1997 (06.06.97)

(30) Priority Data:
60/018,954 7 June 1996 (07.06.96) US

(71) Applicant: ARRAY TECHNOLOGIES [US/US]; 460 Page Mill Road, Palo Alto, CA 94306 (US).

(72) Inventor: HEYNEKER, Herbert, L.; 460 Page Mill Road, Palo Alto, CA 94306 (US).

(74) Agents: CHICKERING, Robert, B. et al.; Flehr Hohbach Test Albritton & Herbert LLP, Suite 3400, 4 Embarcadero Center, San Francisco, CA 94111-4187 (US).

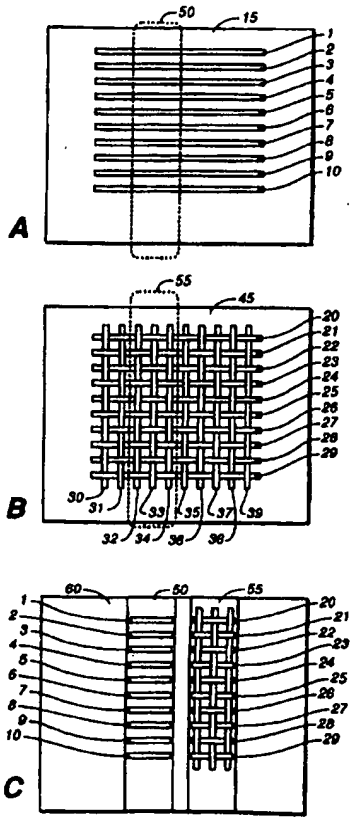
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*
*Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(54) Title: IMMOBILISED LINEAR OLIGONUCLEOTIDE ARRAYS

(57) Abstract

The present invention provides oligonucleotide arrays comprising a solid support comprising a plurality of different oligonucleotide pools. Each oligonucleotide pool is arranged in a distinct linear row to form an immobilised oligonucleotide stripe, wherein the length of each stripe is greater than its width. Composite arrays are also provided comprising at least one strip of a first array and at least one strip of a second array. Furthermore, the invention also provides methods for making the arrays and methods of detecting the presence or absence of a target sequence in a sample.



**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
**C07D 487/04, A61K 31/505, 31/415, C07D 231/40, 401/06**

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(11) International Publication Number: **WO 98/49166**

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(21) International Application Number: PCT/EP98/02257

(22) International Filing Date: 10 April 1998 (10.04.98)

(30) Priority Data:

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| 9708406.5 | 25 April 1997 (25.04.97) | GB |
| 9715380.3 | 22 July 1997 (22.07.97) | GB |
| 9722954.6 | 30 October 1997 (30.10.97) | GB |

(71) Applicant *(for GB only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for all designated States except GB US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BUNNAGE, Mark, Edward [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). MATHIAS, John, Paul [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). STREET, Stephen, Derek, Albert [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). WOOD, Anthony [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: HAYLES, James, Richard et al.; Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

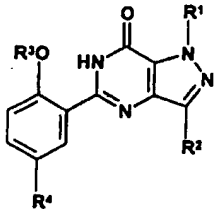
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

**Published**

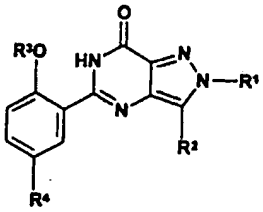
*With international search report.*

*Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(54) Title: PYRAZOLOPYRIMIDINONES WHICH INHIBIT TYPE 5 CYCLIC GUANOSINE 3',5'-MONOPHOSPHATE PHOSPHODIESTERASE (cGMP PDE5) FOR THE TREATMENT OF SEXUAL DYSFUNCTION



(IA)



(IB)

(57) Abstract

Compounds of formulae (IA) and (IB) or pharmaceutically or veterinarily acceptable salts thereof, or pharmaceutically or veterinarily acceptable solvates of either entity, wherein $R^1$ is $C_1$ to $C_3$ alkyl substituted with $C_3$ to $C_6$ cycloalkyl, $CONR^5R^6$ or a N-linked heterocyclic group; $(CH_2)_n$Het or $(CH_2)_n$Ar; $R^2$ is $C_1$ to $C_6$ alkyl; $R^3$ is $C_1$ to $C_6$ alkyl optionally substituted with $C_1$ to $C_4$ alkoxy; $R^4$ is $SO_2NR^7R^8$; $R^5$ and $R^6$ are each independently selected from H and $C_1$ to $C_4$ alkyl optionally substituted with $C_1$ to $C_4$ alkoxy, or, together with the nitrogen atom to which they are attached, form a 5- or 6-membered heterocyclic group; $R^7$ and $R^8$, together with the nitrogen atom to which they are attached, form a 4-$R^{10}$-piperazinyl group; $R^{10}$ is H or $C_1$ to $C_4$ alkyl optionally substituted with OH, $C_1$ to $C_4$ alkoxy or $CONH_2$; Het is an optionally substituted C-linked 5- or 6-membered heterocyclic group; Ar is optionally substituted phenyl; and n is 0 or 1; are potent and selective cGMP PDE5 inhibitors useful in the treatment of, *inter alia*, male erectile dysfunction and female sexual dysfunction.

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/16966

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(30) Priority Data:

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| 08/912,885 | 15 August 1997 (15.08.97) | US |
| 08/947,779 | 9 October 1997 (09.10.97) | US |
| 08/959,365 | 28 October 1997 (28.10.97) | US |

(71) Applicant *(for all designated States except US)*: HYSEQ, INC. [US/US]; 670 Almanor Avenue, Sunnyvale, CA 94086 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: DRMANAC, Radoje [YU/US]; 850 East Greenwich Place, Palo Alto, CA 94303 (US). DRMANAC, Snezana [YU/US]; 850 East Greenwich Place, Palo Alto, CA 94303 (US). BAIDYA, Narayan [IN/US]; 966 Helen Avenue #1, Sunnyvale, CA 94086 (US).

(74) Agents: ABRAMS, Samuel, B. et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).

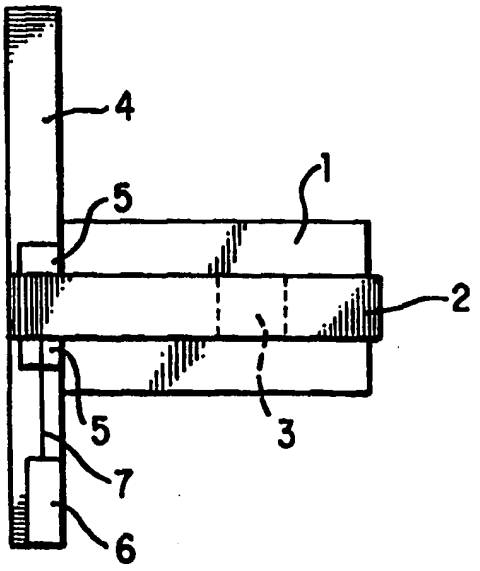
(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*

(54) Title: METHODS AND COMPOSITIONS FOR DETECTION OR QUANTIFICATION OF NUCLEIC ACID SPECIES

(57) Abstract

The present invention provides a method for detecting a target nucleic acid species using an array of probes affixed to a substrate and a plurality of labeled probes. The invention also relates to oligonucleotide probes attached to discrete particles wherein the particles can be grouped into a plurality of sets based on a physical property. A different probe is attached to the discrete particles of each set, and the identity of the probe is determined by identifying the discrete particles from their physical property. The invention further relates to methods using agents which destabilize the binding of complementary polynucleotide strands (decrease the binding energy) or increase stability of binding between complementary polynucleotide strands (increase the binding energy). The figure is an illustration of an apparatus for mass producing probe arrays.



**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C12Q 1/68, C12P 19/34, C07H 21/02, 21/04 — A1

(11) International Publication Number: **WO 99/51773**

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(22) International Filing Date: 31 March 1999 (31.03.99)

(30) Priority Data:
60/080,686 3 April 1998 (03.04.98) US

(71) Applicant: PHYLOS, INC. [US/US]; 128 Spring Street, Lexington, MA 02421 (US).

(72) Inventors: KUIMELIS, Robert, G.; 21 Malbert Road, Brighton, MA 02135 (US). WAGNER, Richard; 1007 Lowell Road, Concord, MA 01742 (US).

(74) Agent: ELBING, Karen, L.; Clark & Elbing LLP, 176 Federal Street, Boston, MA 02110-2214 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*

(54) Title: ADDRESSABLE PROTEIN ARRAYS

(57) Abstract

Disclosed herein are arrays of nucleic acid–protein fusions which are immobilized to a solid surface through capture probes which include a non–nucleosidic spacer group and an oligonucleotide sequence to which the fusion (such as an RNA–protein fusion) is bound. Also disclosed herein are solid supports on which these arrays are immobilized as well as methods for their preparation and use (for example, for screening for protein–compound interactions such as protein–therapeutic compound interactions).

**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 487/04, A61K 31/505, C07D 401/12 | A1

(11) International Publication Number: **WO 99/54333**

(43) International Publication Date: 28 October 1999 (28.10.99)

(21) International Application Number: PCT/IB99/00519

(22) International Filing Date: 25 March 1999 (25.03.99)

(30) Priority Data:

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| 9808315.7 | 20 April 1998 (20.04.98) | GB |
| 9814187.2 | 30 June 1998 (30.06.98) | GB |

(71) Applicant *(for all designated States except GB US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(71) Applicant *(for GB only)*: PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(72) Inventors; and

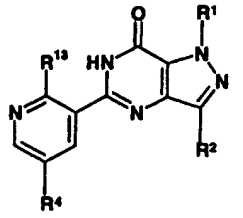
(75) Inventors/Applicants *(for US only)*: BUNNAGE, Mark, Edward [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). MATHIAS, John, Paul [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). STREET, Stephen, Derek, Albert [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). WOOD, Anthony [GB/GB]; Pfizer Central Research, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: SPIEGEL, Allen, J. et al.; Pfizer Inc., 235 East 42nd Street, New York, NY 10017 (US).

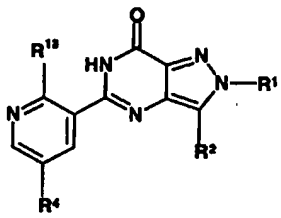
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*

(54) Title: PYRAZOLOPYRIMIDINONE CGMP PDE5 INHIBITORS FOR THE TREATMENT OF SEXUAL DYSFUNCTION



( IA )



( IB )

(57) Abstract

Compounds of formulae (IA) and (IB) wherein $R^1$ is $C_1$ to $C_3$ alkyl optionally substituted with phenyl, Het or a N–linked heterocyclic group selected from piperidinyl and morpholinyl; wherein said phenyl group is optionally substituted by one or more substitutents selected from $C_1$ to $C_4$ alkoxy; halo; CN; $CF_3$; $OCF_3$ or $C_1$ to $C_4$ alkyl wherein said $C_1$ to $C_4$ alkyl group is optionally substituted by $C_1$ to $C_4$ haloalkyl or haloalkoxy either of which is substituted by one or more halo atoms; $R^2$ is $C_1$ to $C_6$ alkyl and $R^{13}$ is $OR^3$ or $NR^5R^6$, or pharmaceutically or veterinarily acceptable salts thereof, or pharmaceutically or veterinarily acceptable solvates of either entity are potent and selective inhibitors of type 5 cyclic guanosine 3',5'–monophosphate phosphodiesterase (cGMP PDE5) and have utility in the treatment of, inter alia, male erectile dysfunction (MED) and female sexual dysfunction (FSD).

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
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(71) Applicant *(for GB only)*: **PFIZER LIMITED** [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant *(for all designated States except GB, US)*: **PFIZER INC.** [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **BROWN, David, Graham** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **GROOM, Colin, Roger** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **HOPKINS, Andrew, Lee** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **JENKINS, Timothy, Mark** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **KAMP, Sarah, Helen** [GB/GB]; U.K. Patent Department, Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **O'GARA, Margaret, Mary** [IE/FR]; Pfizer Global Research and Development, 3-9, rue de la Loge, B.P. 100, F-94265 Fresnes Cedex (FR). **RINGROSE, Heather, Joan** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **ROBINSON, Colin, Mark** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). **TAYLOR, Wendy, Elaine** [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

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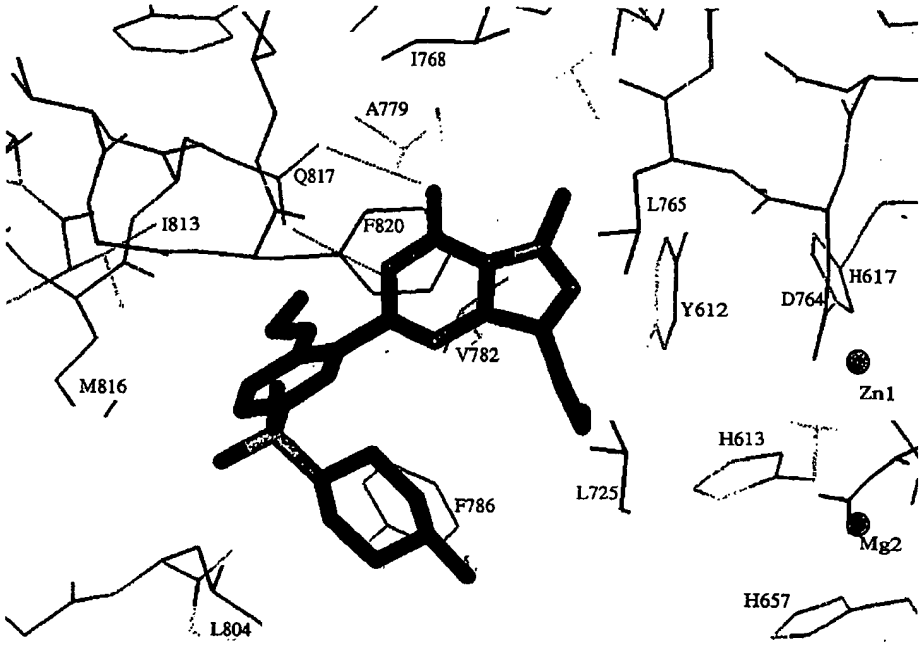
(54) Title: CRYSTAL STRUCTURE OF PHOSPHODIESTERASE 5 AND USE THEREOF




(57) Abstract: The present invention relates , *inter alia* to the crystal structures of a phosphodiesterase 5 (PDE5) and PDE5/PDE5 ligand complex and their uses in identifying PDE5 ligands, including PDE5 inhibitor compounds. The present invention also relates to methods of identifying such PDE5 inhibitor compounds and their medical use. Also contemplated by the present invention are crystals of PDE5/PDE5 inhibitor complexes.

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